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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Group:	1639
Confirmation No.:	9323
Application No.:	10/612,298
Invention:	PEPTIDES COMPRISING AROMATIC D-AMINO ACIDS AND METHODS OF USE
Applicant:	Byron Anderson
Filed:	July 2, 2003
Attorney Docket:	45240-105719
Examiner:	Christopher M. Gross

INTERVIEW SUMMARY

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

During the telephonic interview of September 10 and 12, 2007, the inventor, Dr. Anderson, explained the hypothesis underlying the invention claimed in the application captioned above and explained why the claims are not obvious. If necessary, these comments can be submitted as a Declaration. The advantages of using aromatic proteins were presented and related data in the specification was discussed. Here we will briefly outline the non-obvious arguments discussed with Examiner Christopher Gross:

1. The aromatic amino acid R groups are unique in being able to non-covalently bond with both hydrophobic R groups of other aromatic R groups (the R groups of the amino acids phenylalanine, tyrosine, tryptophan and histidine) as well as other amino acid hydrophobic R groups (e.g., valine, leucine, isoleucine), and with hydrophilic amino acid R groups (e.g., aspartic acid, lysine, threonine) because of the unique nature of the partial electronic charges of the aromatic rings; i.e., the delta negative charge about the faces of the aromatic rings and the delta positive charges about the periphery of the rings. This property of the aromatic R groups is understood only by a small number of biochemists – to our knowledge there is no literature or patent document which relies upon this information to formulate an invention.

Dr. Anderson explained to Examiner Gross the physical-chemical nature of the aromatic R groups that yield these properties. The result of this ability is that the aromatic R groups can form non-covalent bonding interactions in binding sites which are mainly of either hydrophilic or hydrophobic natures.

2. Because the aromatic amino acid R groups are mainly hydrophobic as defined in a water based solvents, the non-covalent bonds formed are of the van der Waals type. However, the hydrophobic aromatic rings also result in the important "hydrophobic effect" contribution to the free energy change of binding. Dr. Anderson reminded Examiner Gross of this effect which adds the important entropic contribution to molecular interactions. The entropic effect can be quite considerable to the binding affinities of molecular interactions. We discussed that, e.g., this hydrophobic effect is one of the main determinants for the three-dimensional structures that newly synthesized protein sequences assume.

For these reasons, it was not a recognized possibility that relatively hydrophobic aromatic amino acid peptides could, in theory, bind into protein binding sites that are either largely hydrophilic or hydrophobic in nature, and thus even protein binding sites that have as their primary ligands carbohydrate (hydrophilic) sequence molecules.

3. Dr. Anderson explained to Examiner Gross that it was the inventive, unexpected and unique findings of the data of the patent application, that the aromatic peptides of the combinatorial library described, exhibited both very high selectivities

of binding to the proteins tested as well as very high affinities.

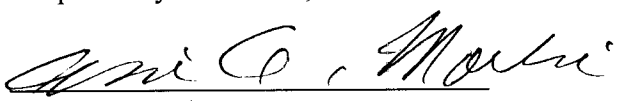
We are unaware of any other publication or patent description that describes the combinatorial aromatic library and the uses of identifying particular aromatic peptide sequences that bind with high affinities and selectivities to diverse proteins.

The data of the patent application also showed that the selective and high affinity of binding could be used to alter the biologic activity of a particular toxin, the botulinum toxin serotype A.

The Examiner, in his Office communication re the interview of Sept., 12, 2007, related the general nature of the discussion to be of substance to "aromatic d peptide binding to *carbohydrate binding proteins* (emphasis provided)." The examples in the patent application were not limited to carbohydrate binding proteins but also described the selectivity of certain aromatic sequences binding the proteins TNFalpha and TGFbeta, as well as the "protective antigen" of anthrax toxin (the protein of the anthrax toxin that binds to target cells and allows other protein factors to then exert the toxic effects). None of the latter proteins has a carbohydrate binding site, but rather each binds to another protein receptor site to effect their biochemical, physiologic effects. Since the patent application, the inventor found 3 other examples of target proteins, that do not bind carbohydrate ligands, and that have binding selectivities to aromatic sequences of the combinatorial aromatic peptide library.

Please allow pending claims.

Respectfully submitted,



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